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(57) Abstract

The present invention concerns a film for medical use consisting of linear block polymers of polyurethane urea containing hydrolysable ester groups. These ester groups must be so spaced from each other on the carbon chain that on their hydrolysis such small fragments are formed that they can be secreted from a human body or that of a mammal. The film is characterised in that it is porous with an average pore size of up to 600 μm. The invention also includes a procedure for the production of the film in which a solution of the film-forming polymers with a concentration of 5-30 % is applied as a thin layer on a surface after which the solvent is evaporated and/or the layer is treated with a polymer-precipitating agent.

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A FILM FOR MEDICAL USE, CONSISTING OF LINEAR BLOCK POLYMERS OF POLYURETHANE AND A METHOD FOR THE PRODUCTION OF SUCH A FILM.

TECHNICAL FIELD

The present invention refers to a film for medical use which film consists of linear block polymers of polyurethane urea containing groups which can be hydrolysed. The film according to the invention is porous and is designed to be used as a temporary implant after operations on, or damage to, a human body or a mammal. The invention particularly includes a procedure for obtaining the desired porosity.

STATE OF THE ART

Healing of living tissue after an operation or damage means that complicated processes are set in motion involving a range of different cell types. In rough outline, the following processes take place in the following order: first a matrix of fibrin is formed, then the epicells begin to divide and bridge over the injury. Under the epithelial layer fibroblasts are already beginning to build connective tissue consisting of collagen and base substance. So gradually the connective tissue is vascularised and condensed into scar tissue.

In other cases, for example healing of broken bones, the formation of the matrix is followed by growth of stem cells, which are categorised as chondroblasts. These form soft callus, consisting of cartilage, in the fracture. Fibroblasts migrate into the cartilage and form zones of collagen. Then osteoblasts enter and form new spongy bone. The final phase in the healing consists of the conversion to hard bone and restoration of the remaining structure. This can take years before it is completed.

THE TECHNICAL PROBLEM

Even if the healing process in general goes well its complicated course gives many possibilities for going wrong. So for example, micro-organisms can affect it or a wounded area can act together with wrong "neighbouring areas" and form a joint growth. Often there are fibroblasts which grow quickly and are a source of unwanted connective tissue formation. This can prevent reconstruction of bone tissue or other desired tissue.

THE SOLUTION

Therefore, there has long been a wish to be able to assist the self-healing process and overcome the problems given above. This has given rise, according to the present invention, to a film which can be used for medical purposes consisting of linear block polymers of polyurethane urea containing hydrolysable ester groups at such a spacing in the carbon chain that on hydrolysis of the ester groups such small fragments are formed that they can be secreted from a human body or that of a mammal, which film is characterised in that it is porous with an average pore size up to 600 μm.

According to the invention the film is further characterised in that the porosity can be varied across the thickness of the film.

According to the invention the porosity through the thickness of the film can be asymmetric, i.e. a thin outer layer has lower porosity.

According to the invention it is often appropriate that the film is laminated with a mesh of biodegradable material.

According to the invention the film can be made up of a coating on the individual threads in a biodegradable mesh or the like.

The invention also includes a procedure for the production of film for medical use consisting of linear block polymers of polyurethane containing hydrolysable ester groups which procedure is characterised in that a solution of the polymers with a concentration of 5-30% is applied in a thin layer on a surface, after which the solvent is evaporated and/or the layer is treated with a polymer-precipitating agent.

According to the invention the precipitating agent can be best chosen from the group consisting of water, methanol and acetone.

According to the invention the porosity is adjusted by means of the polymer concentration, where high concentrations give small pores, by means of the solvent, where highly volatile solvents give small pores, by means of temperature, where high temperatures give small pores and/or time, where short evaporation or precipitation times, as appropriate, give small pores.

According to the invention a mixture of two or more solvents with different volatilities can be used to effect variable porosity through the film thickness.

According to the invention the porosity of the film can also be adjusted by the conditioning of an already-formed film by immersing it in a solvent or a mixture of solvents and non-solvents and/or heat treatment.

Porous films can assist in preventing undesired growth of cells by acting as a barrier over a wound area. In addition porous films can be used to repair or replenish a periosteum in the case of transplants of eg. cartilage. The porosity allows transport of dissolved substances, such as metabolites and/or proteins through the film. If the pore size is sufficient certain cell types can also grow in the film. Films with very large pores can also permit vascularisation. For these various processes the following limiting values for the average pore sizes can be given:

< 1 μm diffusion of dissolved components and growth of collagen,
< 5 μm no growth of fibrous tissue,
< 15 μm relatively little growth of fibrous tissue,
40-200 μm growth of fibrous tissue plus vascularisation,
> 600 μm reduced growth of cells and necrosis of tissue.

The polymer used in the films is degradable to harmless substances which are eliminated from the body by secretion or metabolising. According to the invention the time for degradation is not too short so that one is able to avoid locally high concentrations of degradation products. The speed of degradation is varied also in order to suit the need in various applications.

The requirements for the mechanical properties of the films can vary depending on the application. In many applications the tear strength is especially important, eg. when the films are to be fixed with pins or the like or sewn firmly. In cases which are very demanding, the modulus of

elasticity, tear strength, etc. can be improved by laminating to a mesh of biodegradable fibres. Alternatively, the mesh can be impregnated or coated with a solution or dispersion of the polymer with subsequent removal of the solvent.

DETAILED DESCRIPTION OF THE INVENTION

Polymers

It has become evident that porous films and sheets with the desired properties can be produced from polymers of the type linear block polymers of polyurethane urea. Suitable polymers are produced by use of diisocyanates, diols and carbon chain lengtheners according to methods known for the specific components. In order to form films the molecular weight of the polymers should be > 10,000 Daltons, preferably > 100,000 Daltons.

A convenient technique to produce the polymers is to use the so-called pre-polymerisation technique, i.e. first produce an isocyanate-terminated pre-polymer and thereafter lengthen its carbon chain with a diamine so that the desired molecular weight is obtained. The equations for the reaction can be written as:

$$2\ OCN\text{-}R_1\text{-}NCO + HO\text{-}R_2\text{-}OH \Rightarrow OCN\text{-}R_1\text{-}NHCO\text{-}O\text{-}R_2\text{-}O\text{-}CONH\text{-}R_1\text{-}NCO \quad (1)$$

$$OCN\text{-}R_1\text{-}NHCO\text{-}O\text{-}R_2\text{-}O\text{-}CO\text{-}NH\text{-}R_1\text{-}NCO + NH_2\text{-}R_3\text{-}NH_2 \text{ ---}$$

$$\text{---} \text{-}[\text{-}CONH\text{-}R_1\text{-}NHCO\text{-}O\text{-}R_2\text{-}O\text{-}CONH\text{-}R_1\text{-}NHCONH\text{-}R_3\text{-}NH\text{-}]_n \text{-} \quad (2)$$

where at least one of R_1, R_2 and R_3 must contain one or more ester groups in the carbon chain in order to meet the requirement for degradability into small fragments. It is also possible to use mixtures of several pre-polymers in order to achieve special effects, eg. to introduce groups which can react after polymerisation to introduce physiologically active groups into the polymers. In addition small quantities of carbon chain terminators can be added to limit the upper molecular weight.

The diisocyanates which can be used are diphenylmethane-4,4'-diisocyanate (MDI), dicyclohexylmethane-4,4'-diisocyanate, cyclohexyl-1,4-diisocyanate, toluylene diisocyanate and many more commercially available diisocyanates and laboratory-produced species eg. those based on amino acids, eg. l-lysine methyl ester diisocyanate.

The diolefines used can be simple aliphatics, such as ethylene glycol, diethylene glycol or higher oligomers, tetramethylene oxide glycol or higher oligomers, diol esters such as oligocaprolactone diol, oligoethylene glycol adipate diol, oligodiethylene glycol adipate, dimethylol propionic acid, dimethylol propionic acid methyl ester, trimethylol propane monoallyl ether and many more.

Carbon chain extenders can be simple diamines, such as ethylene diamine, 1,3-propylene diamine or 1,2-propylene diamine. They can also contain ester groups in the carbon chain in order to permit degradation by hydrolysis. It is possible and often expedient to use mixtures of carbon chain extenders.

Primary or secondary monoamines can be used as carbon chain terminators, eg. diethylamine, morpholine or propylamine. Here also, mixtures can be expedient.

Reaction 1 in the reaction scheme given above can be carried out in bulk at elevated temperatures eg. 70-80°C for MDI or 100-110°C for dicyclohexylmethane diisocyanate. In the presence of a catalyst the reactions can be carried out at significantly lower temperatures. However, reaction 2, the carbon chain lengthening, is performed in solution on account of the high speed of reaction and the gelling tendency of the polymer formed. The resulting polymer solution can be used directly or after dilution for the production of film or sheet. In certain solvents, eg. acetone, the polymer so formed is precipitated and can be filtered off and then re-dissolved in a solvent for the same, eg. dimethyl formamide, dimethyl sulphoxide or dimethyl acetamide.

The films

The films are formed from solutions which are applied as thin layers on a plane surface after which the solvent is evaporated and/or the film is treated with a precipitating agent. To obtain a porous film the polymer concentration must be 5-30% preferably 10-20%. After application

the solvent can be wholly or partially evaporated or removed by addition of an anti-solvent. Examples of such are water, methanol and acetone.

A prerequisite for porosity is that the polymer solution at some stage of removal of the solvent forms a gel, i.e. coagulates. Polymers according to the invention have a pronounced tendency for this by the strong interaction of the blocks via phase separation and hydrogen bonding. Important other factors, which favour gel formation, are high polymer concentration and high molecular weight.

Pore size and pore size distribution can be adjusted with concentration and the precipitation conditions associated with addition of the anti-solvent. Alternatively, a pre-produced film can be conditioned with solvent, mixtures of solvents and anti-solvents and/or thermal treatment. Conditioning is carried out by dipping a pre-produced film into solvent which is later allowed to evaporate or by warming up, whereby the film swells up. In this way the pore sizes and their distribution are adjusted to the desired values.

The films according to the invention can be produced from polymer solutions in several ways. The simplest is piece by piece production on a surface, eg. a glass plate, onto which a layer of polymer solution of controlled thickness is spread with an applicator, after which the solvent is removed by evaporation or precipitation under carefully controlled conditions. Continuous production can be carried out by applying the polymer solution to a moving band which carries the material to a zone for precipitation and thereafter to one or more zones for post treatment and final removal of the film from the band which is returned.

The film strength can be increased by stretching. This causes orientation of the polymer molecules and alteration of the sizes and form of the pores. As a result, the strength increases in the direction of stretching. With biaxial stretching the strength in two dimensions can be increased.

An alternative way of increasing the strength of the films is to combine them with a mesh of degradable fibres of, for example, polyurethane urea according to the description in Swedish patent No: 505703. This discloses that the mesh can be partly laminated with a previously prepared film or impregnated or the mesh strengthened with polymer solution followed by evaporation of solvent and/or precipitation according to the methods described above.

A method of producing porous film on curved surfaces is by dipping. For this a former, for example a pipe sealed at one end, is dipped

into a polymer solution. The former is taken out and the polymer is converted to the solid form by evaporation of solvent and/or coagulation with an anti-solvent. The procedure can be repeated until the desired film thickness is obtained, after which the film is slid off the former.

Examples

Example 1: A pre-polymer was produced by reacting diphenylmethane diisocyanate (MDI) with polycaprolactone diol (molecular weight 530) in the molar ratio 2:1 at 70-80°C for 2 hours. 32.35 g of the resulting pre-polymer were dissolved in 138 g of dimethyl formamide (DMF) and the chain extended with 2.35 g of 1,3 diaminopropane and 0.08 g of dibutyl amine in 59 g of DMF at 0°C. The solution was diluted with 12.5% and 1% LiCl was added to reduce the viscosity.

Part of the resulting polymer solution was spread out on a glass plate to a thickness of 300 μm with the help of an applicator. Part of the solvent was evaporated in a fume cupboard at 20°C over 20 minutes. The film whitened thereby, signifying phase separation. The remainder of the solvent was then removed by washing with water. The film so formed was examined using a scanning electron microscope (SEM) and exhibited throughpores with an average diameter of 2 μm.

Example 2. Part of the polymer solution of example 1 was applied to a glass plate and the solvent evaporated in a fume cupboard at 20°C for 14 hours. The residual DMF was washed away with water. The film so formed had a throughpore structure with pore sizes between 2 and 7 μm.

Example 3. Part of the polymer solution of example 1 was applied to a glass plate and immersed in acetone for 10 minutes whereby the polymer separated out. The acetone and residual DMF were washed away with water. The film so formed had a throughpore structure with pore sizes around 1 μm.

Example 4. Part of the polymer solution of example 1 was applied to a glass plate. Part of the solvent was evaporated by warming the glass plate in two minutes up to 100°C. The remaining solvent was evaporated in a fume cupboard in one hour at 20°C. The film so formed was washed with

water to take away the remaining DMF. The film so formed had a throughpore structure with pore sizes between 2 and 7 μm.

Example 5. 12.3 g of the pre-polymer obtained in example 1 were dissolved in 52.5 g of dimethyl formamide (DMF) and had the chain extended with 0.9 g of 1,3-diaminopropane and 0.06 g of dibutylamine in 22.5 g of DMF at 20°C.

Part of the resulting polymer solution was applied to a glass plate to a thickness of 500 μm with the help of an applicator. The solvent was evaporated in a fume cupboard for 14 hours at 20°C. The residual DMF was washed away with water.

Example 6. A pre-polymer was produced by reacting dicyclohexane methane diisocyanate (H_{12}MDI) with polycaprolactone diol (molecular weight 530) in the molar ratio 2:1 at 100-110°C for four hours. Additionally, a pre-polymer was produced by reacting H_{12}MDI with dimethylolpropionic acid in the ratio 2:1 in dimethyl sulphoxide (DMSO) at 75-80°C for one hour. 26 g of pre-polymer 1 and 8.7 g of pre-polymer 2+DMSO were dissolved in 66 g of DMSO and the chain extended with 2.12 g of 1,3-diaminopropane in 20 g of DMSO at 20°C.

Part of the resulting polymer solution was applied to a glass plate to a thickness of 300 μm with the help of an applicator. The solvent was evaporated in a fume cupboard for 14 hours at 20°C. The residual DMF was washed away with water.

Example 7. A pre-polymer was produced by reacting diphenylmethane diisocyanate (MDI) with polydiethyleneglycol adipate (molecular weight 550) in the molar ratio 2:1 at 70-80°C for two hours. 13.2 g of the resulting pre-polymer were dissolved in 34 g of dimethylformamide (DMF) and the chain extended with 0.68 g of 1,3-diaminopropane and 0.05 g dibutylamine in 22 g of DMF at 20°C.

Part of the resulting polymer solution was applied to a glass plate to a thickness of 500 μm with the help of an applicator. The solvent was evaporated in a fume cupboard for 14 hours at 20°C. The residual DMF was washed away with water.

Example 8. A pre-polymer was produced by reacting diphenylmethane diisocyanate (MDI) with 3-allyloxy-1,2-propane diol in the molar ratio 2:1 at

70-80°C for two hours. 6.12 g of the resulting pre-polymer and 17.62 g of the pre-polymer prepared in example 7 were dissolved in 65 g of dimethyl sulphoxide (DMSO) and the chain extended with 2.17 g of 1,2-diaminopropane plus 0.07 g of ethylamine in 3.5 g of acetone and 30 g of DMSO at 20°C. The resulting polymer solution was diluted to 15% concentration by addition of 35 g DMSO.

Part of the resulting polymer solution was applied to a glass plate to a thickness of 500 µm with the help of an applicator. The solvent was evaporated in a fume cupboard for 14 hours at 20°C. The residual DMSO was washed away with water.

The invention is not limited to the preparation examples shown since these can be varied in several ways within the scope of the patent claims.

PATENT CLAIMS

1. Film for medical use consisting of linear block polymers of polyurethane urea containing hydrolysable ester groups at such a spacing on the carbon chain that on hydrolysis of the ester groups such small fragments are formed that they can be secreted from a human body or that of a mammal, characterised in that the film is porous with an average pore size of up to 600 µm.

2. Film according to Claim 1, characterised in that the porosity can be varied across the thickness of the film.

3. Film according to Claim 2, characterised in that the porosity in the film thickness is asymmetric.

4. Film according to any of Claims 1-3, characterised in that the film is laminated with a mesh of biodegradable material.

5. Film according to any of Claims 1-3, characterised in that the film forms a coating on the individual threads of a biodegradable fabric or the like.

6. Procedure for the production of a film for medical use consisting of linear block polymers of polyurethane urea containing hydrolysable ester groups, characterised in that a solution of the polymers with a concentration of 5-30%, preferably 10-20% is applied in a thin layer onto a surface, after which the solvent is evaporated and/or the layer is treated with a polymer-precipitating agent.

7. Procedure according to Claim 6, characterised in that the precipitating agent is chosen from a group consisting of water, methanol and acteone.

8. Procedure according to any of Claims 6 or 7, characterised in that the porosity is adjusted by polymer concentration, where high concentrations give small pores, by solvent, where highly volatile solvents give small pores, by temperature, where high temperatures give small pores and/or time, where short evaporation or precipitation times as appropriate give small pores.

9. Procedure according to any of Claims 6-8, characterised in that a mixture of two or more solvents with different volatilities are used to bring about varying porosity through the thickness of the film.

10. Procedure according to any of Claims 6-9, characterised in that pore size in the film can be adjusted by the conditioning of a pre-produced film by immersion in a solvent or mixture of solvents and anti-solvents and/or thermal treatment.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 00/00084

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61L 27/00, C08G 18/10, C08G 18/32
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61L, C08G

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SE 505703 C2 (POLYRAND AB), 29 Sept 1997 (29.09.97), see abstract; page 2, lines 19-28; page 5, lines 30-32; page 10, lines 4-14	1,6
A	WO 8601095 A1 (MEDTRONIC, INC.), 27 February 1986 (27.02.86), see page2, line 29 - page 3, li ne 36; page 4, lines 18-26; page 5, lines 25-31; page 7, line 19 - page 8, line 2; page 8, lines 13-36; page 9, lines 9-15	1-10

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
SE 505703 C2	29/09/97	AU 709440 B	26/08/99
		AU 1154797 A	14/07/97
		CA 2240061 A	26/06/97
		CN 1214057 A	14/04/99
		CZ 9801793 A	11/11/98
		EP 0866816 A	30/09/98
		HU 9901201 A	28/07/99
		IL 124884 D	00/00/00
		NO 982703 A	14/07/98
		NZ 324479 A	28/05/99
		PL 327246 A	07/12/98
		SE 9504495 A	16/06/97
		SK 79798 A	10/03/99
		WO 9722643 A	26/06/97
WO 8601095 A1	27/02/86	AU 573506 B	09/06/88
		AU 4722085 A	07/03/86
		CA 1244725 A	15/11/88
		DE 3585611 A	16/04/92
		EP 0190283 A,B	13/08/86
		SE 0190283 T3	
		JP 6026551 B	13/04/94
		JP 61503008 T	25/12/86
		US 4605406 A	12/08/86